

	L #	Hits	Search Text	DBs
1	L1	61	HISTIDASE	USPAT ; US-PG PUB
2	L2	24	HISTIDINE ADJ AMMONIA ADJ LYASE	USPAT ; US-PG PUB
3	L3	82	L1 OR L2	USPAT ; US-PG PUB
4	L4	74854	VIRUS OR VIRAL	USPAT ; US-PG PUB
5	L5	160688	DISEASE	USPAT ; US-PG PUB
6	L6	66480	CANCER	USPAT ; US-PG PUB
7	L7	13398	IMMUNOSUPPRES\$	USPAT ; US-PG PUB
8	L8	608324	TREATMENT	USPAT ; US-PG PUB
9	L9	636	HISTIDINOL	USPAT ; US-PG PUB
10	L10	42	L3 AND L4	USPAT ; US-PG PUB
11	L11	32	L3 AND L5	USPAT ; US-PG PUB
12	L12	1	L3 SAME L4	USPAT ; US-PG PUB
13	L13	4	L3 SAME L5	USPAT ; US-PG PUB
14	L14	2	L3 SAME L6	USPAT ; US-PG PUB
15	L15	1	L3 SAME L7	USPAT ; US-PG PUB

	L #	Hits	Search Text	DBs
16	L16	1	L3 SAME L8	USPAT ; US-PG PUB
17	L17	4	L12 OR L13 OR L14 OR L15 OR L16	USPAT ; US-PG PUB
18	L18	6	L3 AND L9	USPAT ; US-PG PUB
19	L19	8	L18 OR L17	USPAT ; US-PG PUB

FILE 'REGISTRY' ENTERED AT 10:14:49 ON 25 FEB 2003

=> S HISTIDINE AMMONIA LYASE/CN

L1 0 HISTIDINE AMMONIA LYASE/CN

=> S HISTIDASE/CN

L2 1 HISTIDASE/CN

=> D

L2 ANSWER 1 OF 1 REGISTRY COPYRIGHT 2003 ACS

RN 9013-75-6 REGISTRY

CN Ammonia-lyase, histidine (9CI) (CA INDEX NAME)

OTHER NAMES:

CN E.C. 4.3.1.3

CN ***Histidase***

CN Histidinase

CN Histidine .alpha.-deaminase

CN Histidine ammonia-lyase

CN Histidine deaminase

CN L-Histidase

CN L-Histidine ammonia-lyase

MF Unspecified

CI MAN

LC STN Files: AGRICOLA, ANABSTR, BIOBUSINESS, BIOSIS, BIOTECHNO, CA, CABA,
CAPLUS, CHEMCATS, CSCHEM, EMBASE, IFICDB, IFIPAT, IFIUDB, IPA,
NAPRALERT, TOXCENTER, USPATFULL

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

579 REFERENCES IN FILE CA (1962 TO DATE)

4 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA

579 REFERENCES IN FILE CAPLUS (1962 TO DATE)

FILE 'MEDLINE' ENTERED AT 10:16:38 ON 25 FEB 2003

=> S L2

L3 0 L2

FILE 'CAPLUS' ENTERED AT 10:17:28 ON 25 FEB 2003

=> S L2

L4 580 L2

=> S HISTIDINE AMMONIA LYASE;S HISTIDASE

60516 HISTIDINE

1874 HISTIDINES

61073 HISTIDINE

(HISTIDINE OR HISTIDINES)

157971 AMMONIA

114 AMMONIAS

158029 AMMONIA

(AMMONIA OR AMMONIAS)

14131 LYASE

1885 LYASES

15020 LYASE

(LYASE OR LYASES)

L5 248 HISTIDINE AMMONIA LYASE

(HISTIDINE (W) AMMONIA (W) LYASE)

547 HISTIDASE

15 HISTIDASES

L6 548 HISTIDASE

(HISTIDASE OR HISTIDASES)

=> S L4,L5,L6

L7 765 (L4 OR L5 OR L6)

=> S CORYNEBACTERIA?

L8 661 CORYNEBACTERIA?

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=> S VIRUS AND VIRAL;S TREATMENT;S DISEASE;S CANCER;S IMMUNOSUPPRES?;S HISTIDINOL
    277836 VIRUS
    56756 VIRUSES
    287612 VIRUS
        (VIRUS OR VIRUSES)
    116214 VIRAL
        6 VIRALS
    116220 VIRAL
        (VIRAL OR VIRALS)
L9      96191 VIRUS AND VIRAL

    1747671 TREATMENT
    162577 TREATMENTS
L10     1837031 TREATMENT
        (TREATMENT OR TREATMENTS)

    580885 DISEASE
    160670 DISEASES
L11     659856 DISEASE
        (DISEASE OR DISEASES)

    180457 CANCER
    25234  CANCERS
L12     187639 CANCER
        (CANCER OR CANCERS)

L13     37962 IMMUNOSUPPRES?

    549 HISTIDINOL
    1 HISTIDINOLS
L14     549 HISTIDINOL
        (HISTIDINOL OR HISTIDINOLS)

=> S L7 AND (L9,L10,L11,L12,L13)
L15     118 L7 AND ((L9 OR L10 OR L11 OR L12 OR L13))

=> S L7(6A) (L9,L10,L11,L12,L13)
PROXIMITY OPERATOR LEVEL NOT CONSISTENT WITH
FIELD CODE - 'AND' OPERATOR ASSUMED 'L7(6A)('
L16     118 L7(6A)((L9 OR L10 OR L11 OR L12 OR L13))

=> S L7 AND L9
L17     0 L7 AND L9

=> S L7 AND L10;S L7 AND L11;S L7 AND L12;S L7 AND L13
L18     69 L7 AND L10

L19     42 L7 AND L11

L20     14 L7 AND L12

L21     3 L7 AND L13

=> S L19,L20,L21
L22     56 (L19 OR L20 OR L21)

=> S L18 NOT L22
L23     62 L18 NOT L22

=> D L22 1-56 CBIB ABS;D L23 1-62 TI

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prostate ***cancer*** behavior. Singh, Dinesh; Febbo, Phillip G.; Ross, Kenneth; Jackson, Donald G.; Manola, Judith; Ladd, Christine; Tamayo, Pablo; Renshaw, Andrew A.; D'Amico, Anthony V.; Richie, Jerome P.; Lander, Eric S.; Loda, Massimo; Kantoff, Philip W.; Golub, Todd R.; Sellers, William R. (Department of Adult Oncology, Dana-Farber Cancer Institute, Harvard Medical School, Brigham and Women's Hospital, Boston, MA, 02115, USA). Cancer Cell, 1(2), 203-209 (English) 2002. CODEN: CCAECI. ISSN: 1535-6108. Publisher: Cell Press.

AB Prostate tumors are among the most heterogeneous of ***cancers*** , both histol. and clin. Microarray expression anal. was used to det. whether global biol. differences underlie common pathol. features of prostate ***cancer*** and to identify genes that might anticipate the clin. behavior of this ***disease*** . While no expression correlates of age, serum prostate specific antigen (PSA), and measures of local invasion were found, a set of genes was identified that strongly correlated with the state of tumor differentiation as measured by Gleason score. Moreover, a model using gene expression data alone accurately predicted patient outcome following prostatectomy. These results support the notion that the clin. behavior of prostate ***cancer*** is linked to underlying gene expression differences that are detectable at the time of diagnosis.

L22 ANSWER 2 OF 56 CAPLUS COPYRIGHT 2003 ACS

2001:828415 Document No. 137:89412 Detection of variations in the DNA methylation profile of genes in the determining the risk of ***disease*** . Berlin, Kurt; Piepenbrock, Christian; Olek, Alexander (Epigenomics A.-G., Germany). PCT Int. Appl. WO 2001077373 A2 20011018, 636 pp. DESIGNATED STATES: W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG, TR. (German). CODEN: PIXXD2. APPLICATION: WO 2001-XA1486 20010406. PRIORITY: DE 2000-10019058 20000406; WO 2001-DE1486 20010406.

AB The invention relates to an oligonucleotide kit as probe for the detection of relevant variations in the DNA methylation of a target group of genes. The invention further relates to the use of the same for detg. the gene variant with regard to DNA methylation, a medical device, using an oligonucleotide kit, a method for detg. the methylation state of an individual and a method for the establishment of a model for establishing the probability of onset of a ***disease*** state in an individual. Such ***diseases*** may be: undesired pharmaceutical side-effects; cancerous ***diseases*** ; CNS dysfunctions, injuries or ***diseases*** ; aggressive symptoms or relational disturbances; clin., psychol. and social consequences of brain injury; psychotic disorders and personality disorders; dementia and/or assocd. syndromes; cardiovascular ***disease*** , dysfunction and damage; dysfunction, damage or ***disease*** of the gastrointestinal tract; dysfunction, damage or ***disease*** of the respiratory system; injury, inflammation, infection, immunity and/or anastasis; dysfunction, damage or ***disease*** of the body as an abnormal development process; dysfunction, damage or ***disease*** of the skin, muscle, connective tissue or bones; endocrine and metabolic dysfunction, damage or ***disease*** ; headaches or sexual dysfunction. This abstr. record is one of several records for this document necessitated by the large no. of index entries required to fully index the document and publication system constraints.

L22 ANSWER 3 OF 56 CAPLUS COPYRIGHT 2003 ACS

2001:781102 Document No. 135:328746 Cloning, overexpression and therapeutic uses of bioactive ***histidine*** ***ammonia*** ***lyase*** from Corynebacteriaceae. Sethuraman, Natarajan; Roberts, Joseph; MaCallister, Thomas (ME Medical Enzymes A.-G., Switz.). PCT Int. Appl. WO 2001079469 A2 20011025, 98 pp. DESIGNATED STATES: W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT,

BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG, TR. (English). CODEN: PIXXD2. APPLICATION: WO 2001-US12053 20010413. PRIORITY: US 2000-PV197770 20000414.

AB ***Histidine*** ***ammonia*** ***lyase*** isolated from Corynebacteriaceae can decrease serum histidine levels, induce accumulation of urocanic acid, and is not inhibited by L-histidinol. A full-length gene and encoded amino acid sequences of ***histidine*** ***ammonia*** ***lyase*** from Corynebacteriaceae are disclosed. As a result, ***histidine*** ***ammonia*** ***lyases*** similar to the one isolated from Corynebacteriaceae are uniquely suitable for combination therapy with L-histidinol to treat histidine- and/or histamine-dependent pathologies, for example, infectious viruses, such as human Respiratory Syncytial Virus (RSV), Herpes Simplex Virus (HSV), and Human Immunodeficiency Virus (HIV), as well as ***cancers***.

L22 ANSWER 4 OF 56 CAPLUS COPYRIGHT 2003 ACS

2000:788133 Document No. 134:55008 Hepatic ***histidase*** and muscle branched chain aminotransferase gene expression in experimental nephrosis. Ascencio, Claudia; Tovar, Armando R.; Medina-Campos, Omar N.; Pedraza-Chaverri, Jose; Torres, Nimbe (Departamento de Fisiologia de la Nutricion, Area de Nutriologia Molecular, Instituto Nacional de la Nutricion Salvador Zubiran, Mexico, 14000, Mex.). Life Sciences, 67(23), 2775-2784 (English) 2000. CODEN: LIFSAK. ISSN: 0024-3205. Publisher: Elsevier Science Inc..

AB Protein and amino acid metab. is altered during nephrotic syndrome. However, the expression of the amino acid degrading enzymes has not been well studied. The objective of this work was to assess the expression of hepatic ***histidase*** (Hal) and skeletal muscle mitochondrial branched chain amino transferase (BCATm) in rats with exptl. nephrotic syndrome induced by a single injection of puromycin aminonucleoside (150 mg/kg). Six days after the injection rats were killed and hepatic Hal and skeletal muscle BCATm activities were measured. Also, total mRNA from both tissues was isolated and Hal and BCATm mRNA expression were analyzed by Northern blot. Rats with NS showed a redn. in food intake with respect to the control group. Hepatic Hal activity increased significantly in nephrotic and pair fed rats by 59% compared to control group. This change in activity was assocd. with a corresponding increase in Hal mRNA abundance. On the other hand, skeletal muscle BCATm activity and mRNA abundance were similar in the three groups studied. These results suggest that the increase in Hal expression was assocd. with the reduced food intake and not to the NS. However, BCAT expression did not change indicating the importance of BCAA in body nitrogen conservation.

L22 ANSWER 5 OF 56 CAPLUS COPYRIGHT 2003 ACS

2000:666621 Document No. 133:256815 Preventives/remedies for digestive ***diseases***. Kimura, Shigeki (Amano Pharmaceutical Co., Ltd., Japan). PCT Int. Appl. WO 2000054800 A1 20000921, 15 pp. DESIGNATED STATES: W: JP, KR, US; RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE. (Japanese). CODEN: PIXXD2. APPLICATION: WO 2000-JP1442 20000309. PRIORITY: JP 1999-65806 19990312.

AB Disclosed are preventives/remedies for digestive ***diseases*** contg., as the active ingredient, at least one of an enzyme hydrolyzing sugar chains having fucose and another enzyme decomp. ammonia. A bacteriostatic method comprises inhibiting or preventing the growth of Helicobacter pylori in a strongly acidic environment by using the above preventives/remedies. As the above enzymes, fucosidase and ***histidase*** are particularly preferable. Thus, the conditions for fixation or growth of H. pylori in the strongly acidic environment are inhibited and thus the growth of H. pylori can be inhibited or prevented.

L22 ANSWER 6 OF 56 CAPLUS COPYRIGHT 2003 ACS

2000:441628 Document No. 133:68969 Assays for ligands for nuclear receptors using peptide sequences. Blanchard, Steven Gerard; Kliever, Anthony; Lehmann, Jurgen; Parks, Derek J.; Stimmel, Julie Beth; Willson, Timothy Mark (Glaxo Group Limited, UK). PCT Int. Appl. WO 2000037077 A1 20000629, 62 pp. DESIGNATED STATES: W: AE, AL, AM, AT, AU, AZ, BG, BR, CA, CH, CN, CU, DE, DK, EE, ES, FI, GB, GD, GH, HR, IN, IS, JP, LK, LU, LV, MD, MN, MW, MX, NO, RU, SD, SE; RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, MR, NE, TD, TG. (English). CODEN: PIXXD2. APPLICATION: WO 1999-US30947 19991222. PRIORITY: US 1998-PV135097 19981223.

AB The present invention provides a method of identifying compds. for the treatment of ***diseases*** or disorders modulated by farnesoid X receptor (FXR), comprising the step of detg. whether the compd. interacts directly with FXR, wherein a compd. that interacts directly with FXR is a compd. for the treatment. A generic approach to assay development for nuclear receptors is presented, using purified ligand binding domains. The concept of generic assay development is extended to develop in vitro assays that detect ligand binding by monitoring ligand-induced changes in receptor heterodimerization. This approach is demonstrated using both scintillation proximity and homogeneous time-resolved fluorimetry (HTRF). Another aspect of the invention is a nuclear receptor peptide assay for identifying ligands. This assay utilizes fluorescence resonance energy transfer (FRET) and can be used to test whether putative ligands bind to FXR. The FRET assay is based upon the principle that ligands induce conformational changes in nuclear receptors that facilitate interactions with coactivator proteins required for transcriptional activation. Binding of the FXR nuclear receptor can result in the alteration of expression of various genes that FXR aids in regulating, including genes involved in lipid absorption and digestion in the small intestine and lipid homeostasis in liver. FXR often functions as a heterodimer with the RXR receptor. The inventive method includes using this technol. to affect bile acid and cholesterol homeostasis such that, ultimately, cholesterol and lipid levels can be modified and in treating ***diseases*** in a mammal, including human, in which regulation of bile acid, cholesterol and lipid levels is important. For example, GW4064 (prepd. in a yield of 98%) was given to Fischer rats at a dose of 30 mg/kg for 7 days. At the end of study, serum triglyceride levels were decreased by 26% compared to a vehicle-treated controls. Nearly 20 genes were identified in the intestine that were regulated >1.5-fold by GW4064. The expression of roughly half of these genes was decreased by GW4064 treatment. All of these down-regulated genes are involved in either lipid absorption or proteolysis, including lipases, proteases, and a colipase.

L22 ANSWER 7 OF 56 CAPLUS COPYRIGHT 2003 ACS

1999:795994 Document No. 132:31744 Gene probes used for genetic profiling in healthcare screening and planning. Roberts, Gareth Wyn (Genostic Pharma Ltd., UK). PCT Int. Appl. WO 9964627 A2 19991216, 745 pp. DESIGNATED STATES: W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG. (English). CODEN: PIXXD2. APPLICATION: WO 1999-GB1780 19990604. PRIORITY: GB 1998-12099 19980606; GB 1998-13291 19980620; GB 1998-13611 19980624; GB 1998-13835 19980627; GB 1998-14110 19980701; GB 1998-14580 19980707; GB 1998-15438 19980716; GB 1998-15576 19980718; GB 1998-15574 19980718; GB 1998-16085 19980724; GB 1998-16086 19980724; GB 1998-16921 19980805; GB 1998-17097 19980807; GB 1998-17200 19980808; GB 1998-17632 19980814; GB 1998-17943 19980819.

AB There is considerable evidence that significant factor underlying the individual variability in response to ***disease***, therapy and prognosis lies in a person's genetic make-up. There have been numerous examples relating that polymorphisms within a given gene can alter the functionality of the protein encoded by that gene thus leading to a variable physiol. response. In order to bring about the integration of genomics into medical practice and enable design and building of a technol. platform which will enable the everyday practice of mol. medicine a way must be invented for the DNA sequence data to be aligned with the identification of genes central to the induction, development, progression and outcome of ***disease*** or physiol. states of interest. According to the invention, the no. of genes and their configurations (mutations and polymorphisms) needed to be identified in order to provide crit. clin. information concerning individual prognosis is considerably less than the 100,000 thought to comprise the human genome. The identification of the identity of the core group of genes enables the invention of a design for genetic profiling technologies which comprises of the identification of the core group of genes and their sequence variants required to provide a broad base of clin. prognostic information - "genostics". The "Genostic" profiling of patients and persons will radically enhance the ability of clinicians, healthcare professionals and

other parties to plan and manage healthcare provision and the targeting of appropriate healthcare resources to those deemed most in need. The use of this invention could also lead to a host of new applications for such profiling technologies, such as identification of persons with particular work or environment related risk, selection of applicants for employment, training or specific opportunities or for the enhancing of the planning and organization of health services, education services and social services.

L22 ANSWER 8 OF 56 CAPLUS COPYRIGHT 2003 ACS

1999:795993 Document No. 132:31743 Gene probes used for genetic profiling in healthcare screening and planning. Roberts, Gareth Wyn (Genostic Pharma Limited, UK). PCT Int. Appl. WO 9964626 A2 19991216, 149 pp. DESIGNATED STATES: W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG. (English). CODEN: PIXXD2. APPLICATION: WO 1999-GB1779 19990604. PRIORITY: GB 1998-12098 19980606; GB 1998-28289 19981223.

AB There is considerable evidence that significant factor underlying the individual variability in response to ***disease***, therapy and prognosis lies in a person's genetic make-up. There have been numerous examples relating that polymorphisms within a given gene can alter the functionality of the protein encoded by that gene thus leading to a variable physiol. response. In order to bring about the integration of genomics into medical practice and enable design and building of a technol. platform which will enable the everyday practice of mol. medicine a way must be invented for the DNA sequence data to be aligned with the identification of genes central to the induction, development, progression and outcome of ***disease*** or physiol. states of interest. According to the invention, the no. of genes and their configurations (mutations and polymorphisms) needed to be identified in order to provide crit. clin. information concerning individual prognosis is considerably less than the 100,000 thought to comprise the human genome. The identification of the identity of the core group of genes enables the invention of a design for genetic profiling technologies.

L22 ANSWER 9 OF 56 CAPLUS COPYRIGHT 2003 ACS

1997:354611 Document No. 127:63765 Histidine metabolic disorders. Wada, Yoshiro (Nagoya City Univ., Japan). Saishin Naikagaku Taikei, Volume 8, 279-286. Editor(s): Imura, Hiroo. Nakayama Shoten: Tokyo, Japan. (Japanese) 1996. CODEN: 64JFAS.

AB A review with 31 refs. on histidine metabolic disorders in humans. The metabolic and mol. basis of histidinemia is described including defects in ***histidase***.

L22 ANSWER 10 OF 56 CAPLUS COPYRIGHT 2003 ACS

1992:463458 Document No. 117:63458 Some molecular mechanisms of dalargin antioxidant action of the liver in conditions of experimental cholestasis. Korotkina, R. N.; Fomchenkov, E. P.; Andreev, V. I.; Smirnova, V. I.; Karelin, A. A. (A. V. Vishnevskii Inst. Surg., USSR). Byulleten Eksperimental'noi Biologii i Meditsiny, 113(1), 38-40 (Russian) 1992. CODEN: BEBMAE. ISSN: 0365-9615.

AB Changes in the antioxidant activity of dalargin in the liver after naloxone (100 .mu.g/kg) administration were examd. in 144 rats with cholestasis. It was found that dalargin inhibited the activity of xanthine oxidase by 32-37% in different time periods after the injection. Dalargin and naloxone when used in combination, had no effect on the enzyme activity. Glutathione-S-transferase activity rose by 38.0% and 21.8% at hours 1 and 3 after the injection, resp., while simultaneous injection of dalargin and naloxone induced no changes in the enzyme activity after 1 h, though it decreased it by 36.8% and 26.4% on hour 3 and 5, resp. Dalargin inhibited lipid peroxidn. by 29-35%, simultaneous injection of dalargin and naloxone raised lipid peroxidn. by 109.2%, 80.7%, and 25.7% after 1, 3 and 5 h, resp. Dalargin injection caused a marked tendency to lowering of blood release of the liver-specific enzymes ***histidase*** and urokinase in line with enhancement of their activity in the liver. A combined injection of dalargin and naloxone promoted high

release of ***histidase*** and urokaninase in blood and did not change ***histidase*** activity in the liver in all cases. Urokaninase activity elevated at 5 h. It was noticed that dalargin raised leu-enkephalin levels in the liver 3.5-fold 1 h after the injection. The reduced dalargin antioxidant effect coupled with naloxone pretreatment demonstrated indirect action of the neuropeptide on the liver via neuronal receptors of the liver.

L22 ANSWER 11 OF 56 CAPLUS COPYRIGHT 2003 ACS

1991:226927 Document No. 114:226927 Dynamics of the enzymic activity involved in metabolism of glutathione in experimental acute cholecystitis. Zhumadilov, Zh. Sh.; Korotkina, R. N.; Karelin, A. A. (A. V. Vishnevskii Inst. Surg., Moscow, USSR). Voprosy Meditsinskoi Khimii, 37(2), 42-4 (Russian) 1991. CODEN: VMDKAM. ISSN: 0042-8809.

AB The activity of glutathione-related enzymes was studied in erythrocytes of dogs with destructive cholecystitis. As clin. symptoms of intoxication developed, the enzymic activity decreased. In animals with purulent inflammatory complications, a distinct decrease was detected in the activity of glutathione reductase (by 54.3%), glutathione S-transferase (by 46.94%), and glutathione peroxidase (by 42.1%). Specific methods should be chosen for the correction of impairments in the enzymic activity to improve the treatment efficiency as well as for the prophylaxis of complications. A procedure developed for the cholecystitis treatment, which involved transport of antibiotics by autologous erythrocyte ghosts, was more effective compared to routine methods, as shown by the animal clin. state and the dynamics of liver-specific (***histidase*** and urocaninase) and glutathione-related enzymes activity. This procedure may be used in clin. practice. The lab. tests described may serve for the evaluation of treatment efficiency.

L22 ANSWER 12 OF 56 CAPLUS COPYRIGHT 2003 ACS

1991:95389 Document No. 114:95389 Effect of dalargin on liver lipid peroxydation. Shloznikov, B. M.; Korotkina, R. N.; Babkina, N. V.; Karelin, A. A. (A. V. Vishnevskii Inst. Surg., USSR). Byulleten Eksperimental'noi Biologii i Meditsiny, 110(12), 609-10 (Russian) 1990. CODEN: BEBMAE. ISSN: 0365-9615.

AB The effect of dalargin (i.p.) on liver lipid peroxidn. and xanthine oxidase activity were studied in rat cholestasis-pancreatitis models at 1, 3, and 5 h after injection. Xanthine oxidase decreased at all periods, and malondialdehyde levels decreased 43.8% at 3 h. Liver ***histidase*** activities at 3 and 5 h were 104.3 and 56.3% of baseline, resp. Blood activities of ***histidase*** and urocanase were also monitored.

L22 ANSWER 13 OF 56 CAPLUS COPYRIGHT 2003 ACS

1991:55668 Document No. 114:55668 Antioxidant effect of dalargin under conditions of acute cholestasis in experiment. Korotkina, R. N.; Fomchenkov, E. P.; Babkina, N. V.; Andreev, V. I.; Shloznikov, B. M.; Karelin, A. A. (Inst. Khir. im. Vishnevskogo, Moscow, USSR). Patologicheskaya Fiziologiya i Eksperimental'naya Terapiya (4), 42-4 (Russian) 1990. CODEN: PAFEAY. ISSN: 0031-2991.

AB Expts. were conducted on 182 rats with acute cholestasis to study the effect of i.p. dalargin injection (10 .mu.g/kg) with the serotonin antagonist ketanserine (150 mg/kg) on xanthine oxidase (XO) activity and lipid peroxidn. in hepatic tissues and on the activity of the hepatospecific enzymes ***histidase*** and urocaninase in hepatic tissues and blood serum 1, 3, and 5 h after the injection. Dalargin alone reduced XO activity by 32-37% in different periods after the injection; dalargin with ketanserine by 37-48%. Dalargin alone reduced the level of lipid peroxidn. by 29-35%; when combined with ketanserine, by 37-49%. The administration of dalargin reveals a distinct tendency towards a decreased release of ***histidase*** and urocaninase into the blood and increase of their activity in the hepatic tissue. Dalargin with ketanserine produced a similar effect but of a higher degree. These data suggest a hepatoprotective effect of dalargin, which is potentiated by ketanserine. Dalargin (50 .mu.g/kg, i.p.) increased the Leu-enkephalin content in the hepatic tissue >3.5-fold 1 h after the injection.

L22 ANSWER 14 OF 56 CAPLUS COPYRIGHT 2003 ACS

1991:40902 Document No. 114:40902 Modulation of lymphocyte proliferation by enzymes that degrade amino acids. Chuang, J. C.; Yu, C. L.; Wang, S. R.

(Dep. Med., Veterans Gen. Hosp., Taipei, 11217, Taiwan). Clinical and Experimental Immunology, 82(3), 469-72 (English) 1990. CODEN: CEXIAL. ISSN: 0009-9104.

- AB Thirteen amino acids were previously demonstrated to be essential and 2 to be partially essential for lymphocyte proliferation. Arginine is one of the essential amino acids, and the highly purified arginase strongly inhibited lymphocyte proliferation. The modulation of lymphocyte growth by various amino acid-degrading enzymes was studied. Peripheral lymphocytes were cultured in RPMI 1640 with or without amino acid-degrading enzyme for 72 h. A total of 17 com. L-amino acid-degrading enzymes were studied. At 10 .mu.g/mL, both lysine decarboxylase and asparaginase completely inhibited lymphocyte proliferation, arginase resulted in 78% inhibition, and tyrosinase 57% inhibition. Other enzymes inhibited less than 20% lymphocyte proliferation: they included alanine dehydrogenase, arginine decarboxylase, aspartase, glutamine decarboxylase, glutamic dehydrogenase, glutaminase, ***histidase***, histidine decarboxylase, leucine dehydrogenase, phenylalanine decarboxylase, phenylalanine hydroxylase, tryptophanase, and tyrosine decarboxylase. All 4 enzymes that strongly inhibited lymphocyte proliferation degraded amino acids that are essential for lymphocyte growth.

L22 ANSWER 15 OF 56 CAPLUS COPYRIGHT 2003 ACS

1988:622837 Document No. 109:222837 Experimental study of the hepatoprotective effect of transcranial transcutaneous electrostimulation and the Leu-enkephalin synthetic analog, dalargin. Kuzin, M. I.; Karelin, A. A.; Korotkina, R. N.; Babkina, N. V.; Shloznikov, B. M. (A. V. Vishnevskii Inst. Surg., Moscow, USSR). Byulleten Eksperimental'noi Biologii i Meditsiny, 106(9), 266-8 (Russian) 1988. CODEN: BEBMAE. ISSN: 0365-9615.

- AB The effects of transcranial transcutaneous electrostimulation (TTES) and(or) dalargin on blood and liver ***histidase*** and urokinase and on liver 5'-nucleotidase were investigated in rats with exptl. cholestasis and pancreatitis. The increases in liver-specific enzymes in the blood and decreases in their content in the liver during liver damage were attenuated by the electroanalgesia and dalargin, due to opioid-mediated stabilization of hepatocyte membranes.

L22 ANSWER 16 OF 56 CAPLUS COPYRIGHT 2003 ACS

1987:615665 Document No. 107:215665 Activity of liver-specific enzymes in experimental intestinal obstruction. Saparov, Sh. S. (Turkm. Gos. Med. Inst., Ashkhabad, USSR). Zdravookhranenie Turkmenistana (11), 25-30 (Russian) 1986. CODEN: ZDTUAB. ISSN: 0513-8736.

- AB Exptl. intestinal obstruction led to increased activity of ***histidase***, tyrosine aminotransferase, and tryptophan pyrrolase in rat livers. The enzyme activity correlated with the severity of ***disease***. There was a direct correlation between the ***histidase*** activity in the liver and blood serum. The prepn. Essenciale (a mixt. of polyunsatd. fatty acids and phospholipids) was effective in correcting the liver enzymic function, by enhancing compensatory resources in the liver and by strengthening hepatocyte membranes.

L22 ANSWER 17 OF 56 CAPLUS COPYRIGHT 2003 ACS

1987:590901 Document No. 107:190901 The influence of some drugs used for combined electroanesthesia and ataralgesia on the appearance of hepatospecific enzymes in the blood. Kuzin, M. I.; Avrutskii, M. Ya.; Karelin, A. A.; Babkina, N. V.; Korotkina, R. N.; Shloznikov, B. M.; Machulin, A. V. (A. V. Vishnevskii Inst. Surg., Moscow, USSR). Byulleten Eksperimental'noi Biologii i Meditsiny, 104(8), 176-8 (Russian) 1987. CODEN: BEBMAE. ISSN: 0365-9615.

- AB Pharmacol. preps. used in conjunction with central transcutaneous elec. stimulation had no pathol. effect in healthy rat livers. In a rat model of cholestasis and pancreatitis there was an increase in blood levels of ***histidase*** and urokinase, assocd. with the development of liver pathol. Fentanyl had the most unfavorable effect on hepatocytes.

L22 ANSWER 18 OF 56 CAPLUS COPYRIGHT 2003 ACS

1986:550815 Document No. 105:150815 Role of organ- and organelle-specific enzymes in diagnosis of chronic hepatitis. Ayubov, A. A.; Sultanova, N. G.; Sultanov, R. G. (Tashk. Med. Inst., Tashkent, USSR). Meditsinskii Zhurnal Uzbekistana (6), 38-40 (Russian) 1986. CODEN: MZUZA8. ISSN:

- 0025-830X.
- AB The shifts in the activity of organelle-specific enzymes in chronic hepatitis patients are correlated to the ***disease*** form and the degree of involvement of hepatocyte organelles in the pathol. process. In chronic persistent hepatitis the changes in enzyme activities are slight but are very marked in chronic active hepatitis. The extent of hepatocyte involvement in the pathol. process is reflected by the activity of the isozyme spectra of lactate dehydrogenase, ***histidase***, fructose 1-phosphate aldolase, and by acid phosphatase in blood serum.
- L22 ANSWER 19 OF 56 CAPLUS COPYRIGHT 2003 ACS
1986:66911 Document No. 104:66911 Activity of liver and blood serum
histidase in experimental intestinal obstruction under sun-heat prostration conditions. Kurbanov, Kh. K.; Babaev, O. G.; Shaparov, Sh. S. (Turk. Gos. Med. Inst., Ashkhabad, USSR). Zdravookhranenie Turkmenistana (4), 12-15 (Russian) 1985. CODEN: ZDTUAB. ISSN: 0513-8736.
- AB In the blood serum of intact rats, ***histidase*** is not normally obsd. In animals with intestinal obstruction, traces of ***histidase*** activity are found in the blood. In the presence of upper-level obstruction (8-10 cm distal from the pylorus), and during the later stages of middle- and lower-level (5-6 cm proximal from the ileocecal angle) obstruction, this activity is somewhat increased. When animals with lower-level obstruction of 24-h duration were subjected to heat prostration (20 min at temps. increasing rectal temp. 3-4.degree.), liver ***histidase*** activity was markedly greater than in animals with obstruction alone. Heating of animals subjected to 72-h obstruction led to even greater increases in liver ***histidase*** activity.
- L22 ANSWER 20 OF 56 CAPLUS COPYRIGHT 2003 ACS
1984:528163 Document No. 101:128163 Effect of Zajdela ascites hepatoma on the activity and synthesis of liver ***histidase*** of tumor-bearing rats. Fedorov, S. A.; Khasigov, P. Z.; Nikolaev, A. Ya. (Dep. Biochem., I. M. Sechenov 1st. Moscow Med. Inst., Moscow, 119435, USSR). Cancer Letters (Shannon, Ireland), 23(1), 67-71 (English) 1984. CODEN: CALEDQ. ISSN: 0304-3835.
- AB The synthesis of ***histidase*** occurs only in free polyribosomes. The relative content of ***histidase*** synthesizing polyribosomes in rat liver, in Zajdela ascites hepatoma cells, and in the liver of tumor-bearing rats is equal to 1.35%, 0.11%, and 0.57%, resp. (of the total amt. of free polyribosomes). Hepatoma cell sap has an inhibitory effect on the synthesis of proteins in the cell-free system reconstructed from polyribosomes and cell sap of control rats.
- L22 ANSWER 21 OF 56 CAPLUS COPYRIGHT 2003 ACS
1984:172696 Document No. 100:172696 Shift of metabolism in rats with ventromedial hypothalamic lesions with respect to changes in daily rhythms of enzyme activity. Nagai, Katsuya; Inoue, Shuji; Ookura, Minoru; Tsujimoto, Hisatoshi; Mori, Tsutomu; Egawa, Masato; Satoh, Shinobu; Nakagawa, Hachiro (Inst. Prot. Res., Osaka Univ., Suita, 565, Japan). International Journal of Obesity, 8(1), 41-51 (English) 1984. CODEN: IJOBDP. ISSN: 0307-0565.
- AB Metabolic alterations in ventromedial hypothalamus (VMH)-lesioned rats were investigated by examg. daily changes of enzyme activities and urea concns. 3 wk after the operation. VMH-lesions in female adult rats caused an elevation in the activity of acetyl-CoA carboxylase in the liver and parametrial adipose tissue. These changes suggest an increased lipogenesis. VMH-lesions also elicited an increase in activities of glucokinase (GK), pyruvate kinase (PK), and fructose 1,6-bisphosphatase (FBPase), and a decrease in activities of phosphofructokinase (PFK), glucose-6-phosphatase (G6Pase), and phosphoenolpyruvate carboxykinase (PEPCK) in the liver. The apparently inconsistent changes in activities of key glycolytic enzymes, GK, PK, and PFK, and key gluconeogenic enzymes, G6Pase, PEPCK, and FBPase in the liver may be explained by the fact that they were favorable for glucose oxidn. through the pentose phosphate cyclic and provide NADPH for lipogenesis in the liver. VMH-lesions induced an increase in urea contents of the liver and serum, and elicited an increase in activity of liver tyrosine aminotransferase (TAT) and a decrease in activity of liver ***histidase***. These changes suggest an accelerated amino acid and protein catabolism, and favor an increment in the supply of the substrate for lipogenesis. Daily rhythms of TAT, ***histidase*** activities and serum urea concn. obsd. in the control

rats were abolished by VMH-lesions, suggesting that VMH-lesions elicit the loss of these daily rhythms, probably through the disturbance of the circadian rhythm of feeding behavior at the dynamic phase (3 wk after operation) of obesity.

L22 ANSWER 22 OF 56 CAPLUS COPYRIGHT 2003 ACS

1983:87150 Document No. 98:87150 Change in an organospecific hepatic enzyme - ***histidase*** - in acute experimental pancreatitis. Synovets, A. S.; Michurin, V. F. (Odess. Med. Inst., Odessa, USSR). Klinicheskaya Khirurgiya (11), 66-7 (Russian) 1982. CODEN: KCLKHAM. ISSN: 0023-2130.

AB In rats with acute pancreatitis (induced by repeated compression of the pancreas or by ligation of the pancreatic ducts) the activity of ***histidase*** in blood serum after 24 h was above normal. Similar changes were obsd. in rats with hepatitis (induced with an i.p. injection of CCl4) or with cholestasis (induced by ligation of the common bile duct). Thus, ***histidase*** of blood serum is a sensitive indicator of direct liver injury or secondary liver injury during acute pancreatitis.

L22 ANSWER 23 OF 56 CAPLUS COPYRIGHT 2003 ACS

1982:57098 Document No. 96:57098 Role of several endogenous factors in the development of contact sensitization industrial allergies. Nalbandyan, G. T. (Tsent. Nauchno-Issled. Kozhno-Venerol. Inst., Moscow, USSR). Vestnik Dermatologii i Venerologii (9), 26-9 (Russian) 1981. CODEN: VDVEAV. ISSN: 0042-4609.

AB Examn. of 525 workers of a large automobile plant in the USSR revealed eczema in 33 and contact dermatitis in 39 workers. These originally nonoccupational ***diseases*** were, however, severely aggravated by occupational factors. All patients had significant increases in the activity of elastase, ***histidase***, and urocaninase in the blood serum, which suggests the pathogenetic role of liver and pancreas disorders in the development of contact sensitization to occupational chem. allergens. After clin. cure or considerable improvement of the skin condition, there was trend towards decreasing activity of the organospecific enzymes.

L22 ANSWER 24 OF 56 CAPLUS COPYRIGHT 2003 ACS

1979:521730 Document No. 91:121730 Evaluation of enzyme tests in ischemic heart ***disease***. Khasanova, R. B.; Levin, A. I.; Petrovich, Yu. A. (Perm. Med. Inst., Perm, USSR). Aktual'nye Problemy Serdechno-Sosudistykh Zabolevanii, 3, 118-21 (Russian) 1977. CODEN: APSZD3. ISSN: 0320-7374.

AB In patients with heart ischemia, serum levels of urocaninase, ***histidase***, sorbitol dehydrogenase, lactate dehydrogenase (LDH), LDH1, and LDH5 were increased, usually in pos. correlation with the severity of the ***disease***. The increases apparently are due to increased permeability of hepatocyte membranes due to hypoxia. Thus, in patients with established liver ***diseases***, the possibility of heart ischemia should be carefully examd.

L22 ANSWER 25 OF 56 CAPLUS COPYRIGHT 2003 ACS

1979:48867 Document No. 90:48867 Effect of the mouse mutants testicular feminization and sex reversal on hormone-mediated induction and repression of enzymes. Bulfield, Grahame; Nahum, Andrew (Inst. Anim. Genet., Univ. Edinburgh, Edinburgh, UK). Biochemical Genetics, 16(7-8), 743-50 (English) 1978. CODEN: BIGEBA. ISSN: 0006-2928.

AB The mouse mutants testicular feminization (Tfm/Y) and sex reversal (Sxr/t,XX) were used to investigate hormone-mediated induction and repression of enzymes. Tfm/Y animals were androgen insensitive, rendering the androgen-inducible enzymes alc. dehydrogenase [9031-72-5] and .beta.-glucuronidase [9001-45-0] noninducible because of an inherited deficiency of a cytosol androgen-receptor complex. The animals displayed female secondary sexual characteristics. Srx/+,XX animals displayed male primary and secondary sexual characteristics with small testes. The Tfm mutation was pleiotropic, preventing repression of an androgen-repressible enzyme, ornithine aminotransferase [9030-42-6], as well as induction of androgen-inducible enzymes. An estrogen-inducible enzyme, histidine decarboxylase [9024-61-7] was not affected by the Tfm mutation. Sxr/+,XX animals produced enough androgen for malelike activities of androgen-sensitive enzymes. Histidine decarboxylase repressed by androgen in normal animals, rather than being unaffected by it in Tfm/Y animals,

was in fact induced. The genetic control of steroid-mediated induction and repression of enzymes is discussed.

L22 ANSWER 26 OF 56 CAPLUS COPYRIGHT 2003 ACS

1978:517007 Document No. 89:117007 Role of pesticides in the occurrence of occupational dermatitis in workers of hothouses. Zolotnikova, G. P.; Somov, B. A. (Inst. Okhr. Tr. Sel'sk. Khoz., Moscow, USSR). Vestnik Dermatologii i Venerologii (4), 76-9 (Russian) 1978. CODEN: VDVEAV. ISSN: 0042-4609.

AB In 26 hothouse workers exposed to phosphamide [60-51-5], kelthane [115-32-2], chlorophos [52-68-6], Acrex [973-21-7], or polycarbazine [9006-42-2] the serum cholinesterase [9001-08-5] activity was inhibited by an av. of 70% and the ***histidase*** [***9013-75-6***] elevated by 73%. Other blood enzymes were less strongly affected. The majority of the workers showed pos. reactions in the lymphocyte blast-transformation and Sp. leukocyte agglomeration tests and neg. responses in the Schelly, Chan, and Nikolaev tests. Blood enzyme fluctuations and immunol. changes were greatest in workers with allergic dermatitis.

L22 ANSWER 27 OF 56 CAPLUS COPYRIGHT 2003 ACS

1978:488331 Document No. 89:88331 Diagnostic importance of changes in the enzymic spectrum of the blood serum in adrenohypercorticism. Kalinin, A. P.; Fekson, E. G. (Mosk. Obl. Nauchno-Issled. Klin. Inst., Moscow, USSR). Terapevticheskii Arkhiv, 50(6), 112-15 (Russian) 1978. CODEN: TEARAI. ISSN: 0040-3660.

AB In 12 patients with Cushing's ***disease***, the serum levels of alanine and aspartate aminotransferases, cholinesterase, acid phosphatase, ***histidase***, glucose-6-phosphatase, and arginase increased 1.9-, 1.5-, 0.5-, 2.5-, 4-, 2.5-, and 4-fold, resp., above normal and those of liver decreased by factors 1, 1.1, 0.8, not given, 2, 2, 1.4, and 1.5, resp., below normal. Thus, the activities in serum usually increased and in liver decreased. In rats with hypercorticism (induced with i.m. injection of 0.5 mg hydrocortisone acetate/100 g body wt. daily for 1 mo) the serum activities of alanine and aspartate aminotransferases, aldolase, alk. and acid phosphatases, ***histidase***, and glucose-6-phosphate increased 7-, not given, not given, 1.5-, 2-, 4.5-, and 3-fold, resp., and those of liver decreased by factors 1.2, 1.2, 1.3, 0.3, 0.8, 1.5, and 0.8, resp. Thus, the pattern of the enzyme changes in serum and liver was similar to that in the patients with Cushing's syndrome. The changes are probably due to the disorder of liver function.

L22 ANSWER 28 OF 56 CAPLUS COPYRIGHT 2003 ACS

1978:440411 Document No. 89:40411 ***Histidase***, urocanase, fructose-1-phosphate aldolase, lactate dehydrogenase, and malate dehydrogenase activity in the blood serum of patients with acute kidney failure. Kirilenko, D. V.; Orlov, M. M.; Zelenkevich, I. B. (Minsk. Med. Inst., Minsk, USSR). Mater. Biokhim. Konf. Pribalt. Resp. B. SSR, 5th, Volume 1, 154-5. Editor(s): Sibul, I. K. Akad. Nauk Est. SSR: Tallinn, USSR. (Russian) 1976. CODEN: 38BKAW.

AB In 22 patients with acute kidney failure, the serum activities of ***histidase*** and urocanase increased from zero to 4.3 and 12.4 units, resp., and those of fructose-1-phosphate aldolase and lactate and malate dehydrogenases increased 13-, 3.-, and 2.3-fold, resp., above normal. The increases of ***histidase*** and urocanase were due to the damage of liver parenchyma; these enzymes can be used for the evaluation of the degree of liver damaged in the kidney failure.

L22 ANSWER 29 OF 56 CAPLUS COPYRIGHT 2003 ACS

1978:20076 Document No. 88:20076 Evaluation of the functional state of the liver in patients with psoriasis. Dyurd, P. I. (Grod. Med. Inst., Grodno, USSR). Zdravookhranenie Belorussii (9), 39-41 (Russian) 1977. CODEN: ZDBEA9. ISSN: 0044-1961.

AB In 32 patients (18-68 yr old) with psoriasis the serum activities of ***histidase*** and urokinase were 0.8-8.3 and 0.8-9.0 units/mL whereas in normal control serums the activities were zero. After treatment the activities decreased but did not disappear. This is probably due to persisting liver damage.

L22 ANSWER 30 OF 56 CAPLUS COPYRIGHT 2003 ACS

1977:482485 Document No. 87:82485 Diagnostic significance of the

- identification of alkaline phosphatase, ***histidase*** and urocanase in the bile of children with ***diseases*** of the hepatobiliary system. Zernov, N. G.; Epikhin, N. V. (Mosk. Med. Stomatol. Inst., Moscow, USSR). *Pediatrica (Moscow)* (3), 56-9 (Russian) 1977. CODEN: PEDTAT. ISSN: 0031-403X.
- AB In children with acute cholecystocholangitis the biliary levels of alk. phosphatase (I), ***histidase*** (II), and urocanase (III) decreased 3-6-, 3-4, and 2-3-fold, resp., below normal. In the subacute disorder, the levels of I increased 1.5-2-fold and those of II and III decreased .apprx.3- and .apprx.2-fold, resp. In the chronic disorder the levels of I increased 3-4-fold and those of II decreased .apprx.twice. In bile duct dyskinesia the levels of I increased .apprx.1.5-fold, and those of II and III decreased 4-6- and 2-3-fold, resp. The detns. are suitable for diagnosis and prognosis of biliary disorders in children.
- L22 ANSWER 31 OF 56 CAPLUS COPYRIGHT 2003 ACS
1977:118949 Document No. 86:118949 Blood enzyme spectrum in ***cancer*** and precancerous ***diseases*** of the stomach. Shukuryan, S. G.; Khachatryan, A. G. (Inst. Rentgenol. Onkol., Yerevan, USSR). *Zhurnal Eksperimental'noi i Klinicheskoi Meditsiny*, 16(4), 71-7 (Russian) 1976. CODEN: ZKMAAX. ISSN: 0514-7484.
- AB In patients with stomach ***cancer*** the serum activities of hexokinase, ***histidase***, and urokinase were higher than those in patients with stomach ulcer; in normal subjects and in patients with chronic gastritis the enzymes were absent. The serum activities of aspartate and alanine aminotransferases, alk. phosphatase, and amidase increased in the sequence: normal subjects < patients with chronic gastritis < stomach ulcer < stomach ***cancer***. In ***cancer*** the levels of all the enzymes were pos. correlated with the stage of the ***disease***.
- L22 ANSWER 32 OF 56 CAPLUS COPYRIGHT 2003 ACS
1977:67240 Document No. 86:67240 Method for determining ***histidase*** activity in small volumes of blood serum. Tabolin, V. A.; Smirnova, T. A.; Burobin, V. A. (II Mosk. Med. Inst., Moscow, USSR). *Laboratornoe Delo* (1), 28-9 (Russian) 1977. CODEN: LABDAZ. ISSN: 0023-6748.
- AB The activity of the organ-specific ***histidase*** of liver was detd. by a micromethod in the umbilical blood serum of 61 newborn children weighing from 1-2.7 kg at birth. The data obtained pointed to the involvement of the liver in children which sustained hypoxia. The suggested method is recommended for wider use in pediatric practice for the purpose of early diagnosis of disturbances of hepatic function.
- L22 ANSWER 33 OF 56 CAPLUS COPYRIGHT 2003 ACS
1977:28282 Document No. 86:28282 Bile enzymes in ***diseases*** of the biliary tract in children. Epikhin, N. V.; Vavilova, T. V. (Mosk. Med. Stomatol. Inst. im. Semashko, Moscow, USSR). *Voprosy Okhrany Materinstva i Detstva*, 21(9), 33-6 (Russian) 1976. CODEN: VOMDAQ. ISSN: 0042-8825.
- AB The activities of alk. and acid phosphatases, lactic dehydrogenase and urocaninase in the bile, were studied in healthy children and children with ***diseases*** of the biliary tract. The activity of alk. phosphatase increased in subacute and chronic cholangitis and acid phosphatase and lactic dehydrogenase activities showed very slight changes. The activities of ***histidase*** and urocaninase displayed some decrease.
- L22 ANSWER 34 OF 56 CAPLUS COPYRIGHT 2003 ACS
1975:576341 Document No. 83:176341 Tryptophan and histidine metabolism during experimental liver failure. Bayandurov, V. G.; Mezhlumyan, L. A. (USSR). *Trudy Erevanskogo Meditsinskogo Instituta*, 16(1), 130-2 (Russian) 1974. CODEN: TEMZAY. ISSN: 0131-937X.
- AB In rats after 1-3 hr of CHCl₃ narcosis, liver tryptophan pyrrolase was immediately decreased and fell to almost zero before death of the animal. Serum ***histidase*** and urocanase was increased in correlation with the degree of destruction of liver parenchyma.
- L22 ANSWER 35 OF 56 CAPLUS COPYRIGHT 2003 ACS
1974:472552 Document No. 81:72552 Hepatoprotective effect of glutamine. Ostroverkhov, G. E.; Khokhlov, A. P.; Malyugin, E. F.; Terent'eva, V. B.; Rykov, V. I.; Reis, B. A.; Burobin, V. A.; Gogiberidze, G. V. (II Mosk. Med. Inst. im. Pirogova, Moscow, USSR). *Terapevticheskii Arkhiv*, 46(1),

89-96 (Russian) 1974. CODEN: TEARAI. ISSN: 0040-3660.

- AB L-glutamine [56-85-9] (200 mg/kg) administered intraportally to dogs stimulated nucleic acid and protein synthesis in the liver, increased the amt. of urea [57-13-6] in the blood, and decreased the activities of ***histidase*** [***9013-75-6***] and urocananase [9014-58-8] in the liver. The amino acid was effective in the treatment of diffuse peritonitis in dogs and against liver damage from chloroform [67-66-3] anesthesia in human patients.

L22 ANSWER 36 OF 56 CAPLUS COPYRIGHT 2003 ACS

1973:490091 Document No. 79:90091 Serum enzymogram during transplantation of the small intestine under experimental conditions. Saburova, L. M.; Kurganskaya, N. N. (Univ. Druzh. Nar. im. Lumumby, Moscow, USSR). Eksperimental'naya Khirurgiya i Anesteziologiya (3), 33-8 (Russian) 1973. CODEN: EKHAFF. ISSN: 0013-3329.

- AB The functional state of the liver after heteropathic allograft of the small intestine into the pelvis was investigated in chronic expts. with dogs divided into 3 series: (1) in allograft of the small intestine without ***immunosuppressive*** therapy; (2) in allograft of the small intestine with ***immunosuppressive*** therapy; (3) in intact dogs with ***immunosuppressive*** therapy. In all series of the expts., an increase of the activity of L-histidine ammonium lyase (I), urocanase (II), fructose-1-phosphate-D-glyceraldehyde-3-phosphate lyase, fructose-1,6-diphosphate-D-glyceraldehyde-3-phosphate lyase, L-alanine-2-ketoglutarate aminotransferase (II), and L-aspartate-2-ketoglutarate aminotransferase in the blood serum was obsd., in some cases as early as 1 week after the transplantation. The acylcholine acylhydrolase activity decreased. In the case of the 2nd series of the expt. 2, the activity of I and II increased in comparison with series 1. The ***immunosuppressive*** therapy (3) series increased the activity of I and II. It was suggested that the detn. of the activity of the enzymes in the blood serum could be used as a sensitive test for the detection of disorders of liver function.

L22 ANSWER 37 OF 56 CAPLUS COPYRIGHT 2003 ACS

1972:497522 Document No. 77:97522 Hepatic activities of 1-carbon enzymes during the chronic administration of diethylnitrosamine, 2-acetylaminofluorene, and N,N-dimethyl-4-aminoazobenzene to rats. Poirier, Miriam C.; Poirier, Lionel A.; Lepage, Raymond (Inst. Cancer Montreal, Hop. Notre-Dame, Montreal, QC, Can.). Cancer Research, 32(6), 1104-7 (English) 1972. CODEN: CNREA8. ISSN: 0008-5472.

- AB Chronic administration to rats of either an hepatocarcinogen (diethylnitrosamine [55-18-5], 2-acetylaminofluorene (I) [53-96-3], or N,N-dimethyl-4-aminoazobenzene (II) [60-11-7]) or a choline [62-49-7]-deficient diet decreased the hepatic levels of 5 enzymes involved in the synthesis of H4-folate formyl derivs.: ***histidase*** (EC 4.3.1.3) [***9013-75-6***], urocanase [9014-58-8], formiminoglutamic acid transferase (EC 2.1.2.5) [9032-83-1], formylase (EC 6.3.4.3) [9023-66-9], and methylene-H4-folate dehydrogenase (EC 1.5.1.5) [9029-14-5]. The relations between the hepatocarcinogens, Me donors, and 1-C compd. metabolism were discussed.

L22 ANSWER 38 OF 56 CAPLUS COPYRIGHT 2003 ACS

1972:473506 Document No. 77:73506 Enzymology of the formation and interconversion of labile 1-carbon groups in five hepatomas and in Walker tumor 256. Lepage, Raymond; Poirier, Lionel A.; Poirier, Miriam C.; Morris, Harold P. (Inst. Cancer Montreal, Hop. Notre-Dame, Montreal, QC, Can.). Cancer Research, 32(6), 1099-103 (English) 1972. CODEN: CNREA8. ISSN: 0008-5472.

- AB The levels of ***histidase***, urocanase, formiminoglutamic acid transferase, dihydrofolate reductase, serine hydroxymethylase, N5,10-methylenetetrahydrofolate dehydrogenase, and formylase, all involved in the metabolism of C1 and related compds., were detd. in the cytoplasmic fractions of 5 rat hepatomas, Walker tumor 256, and livers of tumor-bearing rats. The hepatomas studied included the Novikoff, H-35, and Morris 7800, 7777, and 5123D hepatomas. The activities of virtually all enzymes studied were significantly decreased in hepatomas in comparison to corresponding activities in livers of tumor-bearing rats. The hepatoma levels of formiminoglutamic acid transferase and serine hydroxymethylase never exceeded 7 and 41%, resp., the corresponding enzyme levels found in host liver. The levels of ***histidase***, urocanase,

and dihydrofolate reductase were also significantly lower in all hepatomas studied than in livers of tumor-bearing rats. The levels of formylase in the 5123D hepatoma and of N5,10-methylenetetrahydrofolate dehydrogenase in hepatoma H-35 were comparable to the levels in livers of tumor-bearing rats. In all other hepatomas studied the levels of these two enzymes were lower than in the host livers. With the exception of serine hydroxymethylase, the activities of all enzymes studied were similar in the two rapidly growing tumors, the Novikoff hepatoma and Walker carcinosarcoma 256. No other correlations could be observed between the growth rates of tumors studied and the levels of any enzymes investigated. The results are consistent with an overall decrease in both the C1 and tetrahydrofolate moieties of the labile C1 pool of tumors and with a decreased interconversion of the metabolically labile formyl and hydroxymethyl groups.

L22 ANSWER 39 OF 56 CAPLUS COPYRIGHT 2003 ACS

1972:23640 Document No. 76:23640 Enzyme patterns in a group of transplantable mouse hepatomas of different growth rates. Bresnick, E.; Mayfield, E. D., Jr.; Liebelt, A. G.; Liebelt, R. A. (Dep. Pharmacol., Baylor Coll. Med., Houston, TX, USA). Cancer Research, 31(6), 743-51 (English) 1971. CODEN: CNREA8. ISSN: 0008-5472.

GI For diagram(s), see printed CA Issue.

AB A series of transplantable hepatomas which arose spontaneously in normal mice or in mice treated with gold thioglucose, urethan, or 3-methylcholanthrene (I), was tested for the extent of deviation of the hepatoma enzymic activities from those of normal liver. The growth rates of these hepatomas varied from 21 to 211 days. Deoxythymidine kinase and aspartate transcarbamylase activities correlated to some extent with the growth rate of these hepatomas. Threonine-serine dehydrase, ***histidase***, and carbamylphosphate synthetase activities were almost undetectable in all the hepatomas, while uracil reductase was present in detectable amts. in only 2 of the hepatomas.

L22 ANSWER 40 OF 56 CAPLUS COPYRIGHT 2003 ACS

1971:473469 Document No. 75:473469 Restoration of the cellular function and structure of the liver after obstruction of the bile duct in dogs. Mansurova, I. D.; Antonovich, V. I.; Kaletkina, L. G. (Inst. Gastroenterol., Dushanbe, USSR). Byulleten Eksperimental'noi Biologii i Meditsiny, 71(5), 43-7 (Russian) 1971. CODEN: BEBMAE. ISSN: 0365-9615.

AB Abnormal levels of alk. phosphatase, alanine and aspartate aminotransferases, histidine ammonium lyase, and acetylcholinesterase persisted in the subcellular structures of dog liver even 18 months after spontaneous recanalization of the ligated bile duct, suggesting prolonged metabolic disturbances in the hepatocytes.

L22 ANSWER 41 OF 56 CAPLUS COPYRIGHT 2003 ACS

1969:85673 Document No. 70:85673 Metabolic adaptations during hepatocarcinogenesis. III. Dietary induction of some enzymes of amino acid metabolism during azo dye feeding. Poirier, Lionel A.; Pitot, Henry C. (Med. Sch., Univ. of Wisconsin, Madison, WI, USA). Cancer Research, 29(2), 475-80 (English) 1969. CODEN: CNREA8. ISSN: 0008-5472.

AB N,N-Dimethyl-3'-methyl-4-aminobenzene (I) (0.054% of the diet) was fed to adult male rats (170-190 g.) for 0, 2, 4, or 5 weeks, followed by 5 days on a protein-free diet prior to sacrifice. This treatment produced, at 2-3 weeks, a loss of the metabolic responses of ornithine-.delta.-transaminase (II) and ***histidase*** to dietary induction by casein hydrolyzate (2 ml./100 g.) force-fed at 6, 12, and 18 hrs. before sacrifice, did not alter the induced responses of tryptophan pyrrolase or tyrosine-.alpha.-ketoglutarate-transaminase (III), and decreased the induced level of serine dehydratase (IV). Chronic administration of the carcinogen also decreased the levels of ***histidase*** and II. N,N-Dimethyl-2-methyl-4-aminoazobenzene (V) (0.054% of the diet) fed for 3-5 weeks decreased the induced levels of III and IV only. Rats fed either of the azo dyes showed no wt. gain during the 5 week period, while the av. wt. of controls increased from 187 to 276 g. The liver wts. increased from an av. of 4.59-6.37 g. in controls, to 8.16 g. in rats fed V, but to only 5.70 g. in rats fed I. The liver wt. following casein hydrolyzate intubation increased in controls but not in rats fed either carcinogen.

L22 ANSWER 42 OF 56 CAPLUS COPYRIGHT 2003 ACS

1968:11160 Document No. 68:11160 Enzymology of the liver in patients with chronic ulcerative colitis. Mansurova, I. D. Probl. Gastroenterol., No. 1, 192-204 (Russian) 1966.

AB Biopsies of liver tissue were taken from 78 patients with chronic ulcerative colitis for the detn. of the activity of 10 enzymes (***histidase*** , phosphoglucomutase, ATPase, glucosephosphate isomerase, aldolase, sorbitol dehydrogenase, lactate dehydrogenase, alk. phosphatase, acetylcholinesterase, and choline dehydrogenase) and the content of protein. Decreases of ***histidase*** , sorbitol dehydrogenase, ATPase, aldolase, lactate dehydrogenase, and choline dehydrogenase activities occurred. Activities of alk. phosphatase and acetylcholinesterase were increased. Other enzyme levels were normal. The decrease in activity of choline dehydrogenase correlated with accumulation of fat in the liver. The content of liver protein was decreased, but in 15.3% of the cases the serious disorders in the enzymic activity and drop in protein content were not accompanied by any structural changes in the liver.

L22 ANSWER 43 OF 56 CAPLUS COPYRIGHT 2003 ACS

1967:441851 Document No. 67:41851 Clinical manifestations of histidinase deficiency in children. Kaleva, A.; Krustev, B.; Peev, G. (Katedra Detski Bolesti, Vissh Med. Inst., Plovdiv, Bulg.). Pediatriya (Sofia), 5(6), 548-52 (Bulgarian) 1966. CODEN: PDTAAB. ISSN: 0479-7876.

AB Two cases are described, in which lack of activity of the enzyme histidinase in children was noted. The normal metabolism of histidine is compared with that occurring in the patients which lacked histidinase. In the latter case the blood level of histidine is raised. In the urine are excreted histidine and products of its pathol. metabolism: imidazolepyruvic acid, imidazolelactic acid, and imidazoleacetic acid. The most important manifestations of the ***disease*** are disturbances of speech and retardation of neuropsychic development.

L22 ANSWER 44 OF 56 CAPLUS COPYRIGHT 2003 ACS

1966:450501 Document No. 65:50501 Original Reference No. 65:9475g-h Meaning of biochemical differences between normal and ***cancer*** cells. Potter, Van R. (Univ. of Wisconsin Med. School, Madison). Natl. Cancer Conf., Proc., 5th, Philadelphia, Volume Date 1964 17-25 (English) 1965.

AB The wide variations in the levels, inducibility, and repressibility of enzymes in the process of carcinogenesis could be essential or random. Essential alterations might occur in 2 or more genes. Glucose-6-phosphatase was found in liver parenchyma cells and in minimal deviation hepatoma but was absent in transplantable hepatoma. Tryptophan pyrrolase, ***histidase*** , and transaminases tend to occur in min. deviation hepatoma at levels that resemble newborn rat liver in the transplantation period between 7 and 21 days of age. The activity of threonine dehydrogenase is very low in host liver but high in the hepatoma, even when the protein-to-glucose ratio in the diet is low (Pitot, et al., CA 56, 3982h). Cholesterol synthesis from acetate-14C proceeds at a high level in rat hepatoma even with cholesterol-rich food (Siperstein and Fagan, CA 61, 11123c). 30 references.

L22 ANSWER 45 OF 56 CAPLUS COPYRIGHT 2003 ACS

1966:441454 Document No. 65:41454 Original Reference No. 65:7773g-h, 7774a Spectra of some enzymes and proteins in the liver during different stages in the course of Botkin's ***disease*** . Mansurova, I. D. Aktual'nye Vopr. Patol. Pecheni, Sb. (Dushanbe: Akad. Nauk Tadzh. SSR, Akad. Med. Nauk SSSR, Inst. Kraevoi Med.) 54-60 From: Ref. Zh., Biol. Khim. 1965, Abstr. No. 24F1680. (Russian) 1965.

AB Microchem. studies (2600) on the concn. of enzymes and proteins in the liver of patients with Botkin's ***disease*** were carried out. As controls, liver tissue from 19 patients without liver ***disease*** was examd. Regular changes in the enzyme activities and protein concns. were found to occur, depending upon the phase of the ***disease*** and the severity of involvement of the liver parenchyma. In the initial period of Botkin's ***disease*** , increased activity of alk. phosphatase, cholinesterase, and hexosephosphate isomerase and a decrease in activity of transaminases, sorbitol dehydrogenase, and ***histidase*** were observed in the liver tissue of the patients. At the height of the ***disease*** , the activity of hexosephosphate isomerase and cholinesterase rose still higher (to 59.3 and 90% above normal, resp.) and the activity of ***histidase*** , sorbitol

dehydrogenase, and aldolase decreased significantly. In the convalescent period there was a tendency toward normalization of all enzyme activities. At the beginning of the illness, there was a significantly lower concn. of total protein in liver tissue. At the height of the illness, there was a sharp fall in water-sol. protein. In the period of convalescence, the concn. of total and of water-sol. protein also remained low.

L22 ANSWER 46 OF 56 CAPLUS COPYRIGHT 2003 ACS

1966:406298 Document No. 65:6298 Original Reference No. 65:1185f-h,1186a Investigation of ***histidase*** in acute and chronic ***diseases*** of the liver. Kaletkina, L. G.; Lopatina, L. A. Aktulal'nye Vopr. Patol. Pecheni, Akad. Nauk Tadzh. SSR, Akad. Med. Nauk SSSR, Inst. Kraevoi Med., No. 3, 107-14 (Russian) 1965.

AB The Mardashev-Burobin modification (CA 57, 17006i) of the Tabor-Mehler method for the detn. of ***histidase*** (I) activity is suggested as a diagnostic and prognostic test for liver ***diseases***. Enzyme activity is expressed in micromoles of urocanic acid produced by I during 1 hr. in 1 ml. of blood serum (.times. 102 for convenience). Investigation of human organs for I gave: liver 432, cardiac muscle 108, kidney 56, spleen 12, lungs, brain and intestines 0 micromoles urocanic acid/g. of tissue/hr., indicating that I is chiefly of hepatic origin. I in 20 controls ranged from 0 to 4 micromoles urocanic acid/ml./hr. (mean value 0.1 micromole). Elevated I was found in serums of all patients with liver ***disease***. Highest values were obtained in 2 cases of carcinoma (8.8 and 19.4 micromoles urocanic acid/ml./hr.). Highest I values in examn. of more than 140 patients with acute and chronic liver ***diseases*** were obtained at the climax (3rd week) of epidemic hepatitis (mean value 7.5) and in active forms of chronic hepatitis (6.62) and cirrhosis of the liver (6.36). A sharp drop of I in mild forms of epidemic hepatitis was found after the 3rd week; more serious cases showed a sustained high level from the 2nd through the 5th weeks. Active forms of epidemic hepatitis were distinguishable from the inactive by a much higher I (6.36 vs. 1.66, resp.). In 17 patients with ulcerative colitis, 2 showed no elevated I, but the 15 severe cases gave high levels. Comparison of I with a histol. study of biopsy material disclosed a close relation between I and the degree of protein dystrophy of the parenchymal cells.

L22 ANSWER 47 OF 56 CAPLUS COPYRIGHT 2003 ACS

1965:39461 Document No. 62:39461 Original Reference No. 62:6986e-f The activity of ***histidase*** under the influence of experimental liver damage and psycho-drugs. Kusch, T. (Friedrich-Schiller Univ., Jena). Acta Biol. Med. Ger., 13(3), 351-7 (German) 1964.

AB Rats were treated with 10 g. of chlorpromazine/100 g. of body wt., 1 mg. of phenelzine/100 g., or 5 mg. of serotonin creatinine sulfate/100 g. with no effect on the ***histidase*** activity in the serum, but only in the liver. However, if the rats were pretreated with ml. of CCl4 intraperitoneally, bile duct occlusion, or sham operations, subcutaneous injections of chlorpromazine, phenelzine, and serotonin creatinine sulfate caused the ***histidase*** activity to increase in the serum, and to decrease in the liver.

L22 ANSWER 48 OF 56 CAPLUS COPYRIGHT 2003 ACS

1964:55087 Document No. 60:55087 Original Reference No. 60:9726b Correlation of the enzymic activity with the metabolism of amino acids during the stages of leukemia. Di Simone, A.; Del Vecchio-Blanco, C.; Barbieri, A. M. (Univ. Naples). Boll. Soc. Ital. Biol. Sper., 39(22), 1344-6 (Italian) 1963.

AB In animals with leukemia various amino acid enzymic detns. were made following inoculation or onset of the ***disease***. Activity studies for arginase, ***histidase***, and glutamic dehydrogenase were performed. In each case the enzyme activity decreased as the condition worsened from 7 to 40 days while the total wt. of the liver increased with the lengthening of the period.

L22 ANSWER 49 OF 56 CAPLUS COPYRIGHT 2003 ACS

1963:431015 Document No. 59:31015 Original Reference No. 59:5621c-e Experimental and clinical studies on serum ***histidase*** activity. Takasugi, Toshio; Tsunematsu, Kiyoshi (Hokkaido Univ. School Med., Sapporo, Japan). Nippon Naika Gakkai Zasshi, 50, 816-26 (Unavailable) 1961.

AB A method for detg. ***histidase*** activity, which was almost specifically confined to liver, was developed. Mix 2.4 ml. of 0.1M pyrophosphate buffer (pH 9.2), 0.5 ml. of 0.02M L-histidine (pH 8.5-9.5), and 0.1 ml. serum, and immediately read the optical density at 277 m.mu.. After a 24-hr. incubation at 37.degree. in a well-stoppered vessel, cool to room temp. and again read the increase in the absorbance at 277 m.mu., which was due to the conversion to urocanic acid. A 0.001 difference in the absorbance was arbitrarily chosen as the activity unit. In normal persons and various patients without hepatic disorder, no significant serum ***histidase*** activity was shown, whereas in the cases of hepatic injury a significant increase was observed. The above clin. result was also reproducible in animal expts. on rabbits and rats. The use of serum ***histidase*** activity was discussed as a sensitive and specific indicator of liver damage.

L22 ANSWER 50 OF 56 CAPLUS COPYRIGHT 2003 ACS

1962:485232 Document No. 57:85232 Original Reference No. 57:17070b-c Sulfhydryl groups and amino acid composition of liver histidine deaminase of normal and ***cancer*** -affected animals. Goryukhina, T. A.; Misheneva, V. S.; Parshin, A. N. (Inst. Onkol., Leningrad). Ukr. Biokhim. Zh., 34, 483-9 (Russian) 1962.

AB Cat liver histidine deaminase (I) was more active than I of other animals; analysis showed that it contained less SH groups than the I of rabbit liver. An increase in the enzymic activity of I in rabbits with Brown-Pierce sarcoma was accompanied by a parallel increase in the no. of SH groups. Therefore, it was assumed that liver I activity depended basically upon the SH groups entering into the compn. of the I active center, and to some extent upon the purity of the enzyme prepn.

L22 ANSWER 51 OF 56 CAPLUS COPYRIGHT 2003 ACS

1962:14894 Document No. 56:14894 Original Reference No. 56:2813f-g Comparative study of histidine deaminase properties in liver of normal and cancerous animals. Parshin, A. N.; Goryukhina, T. A.; Misheneva, V. S. (Inst. Oncol. Acad. Med. Sci. U.S.S.R., Leningrad). Ukrain. Biokhim. Zhur., 33, 514-22 (Unavailable) 1961.

AB Tests were made with cats and rabbits free from ***cancer*** and rabbits having Brown-Pearce sarcoma. Results showed that liver histidine deaminase (I) activity was inhibited by ethylenediaminetetraacetate (II), p-chloromereuribenzoate (III), ferricyanide (IV) iodine, and hydroxylamine. I inhibition by II was counteracted by divalent metals and in particular by ions of Co, Zn, and Mn. Inhibiting effect of III was counteracted by cysteine, IV, iodine, and ascorbic acid. The results indicated that I and II are identical.

L22 ANSWER 52 OF 56 CAPLUS COPYRIGHT 2003 ACS

1961:94681 Document No. 55:94681 Original Reference No. 55:17859e-f Transamination reactions of aromatic amino acids in plasma. Coltorti, M.; Giusti, G.; Di Simone, A.; Budillon, G. (Univ. Naples). Acta Vitaminol., 15, 11-15 (Unavailable) 1961.

AB After CCl4-induced liver necrosis in mice, the histidine-pyruvate, phenylalanine-pyruvate, tyrosine-.alpha.-ketoglutarate, and tryptophan-.alpha.-ketoglutarate transaminases appear in serum, esp. if pyridoxal phosphate is added. p-Hydroxyphenylpyruvate oxidase and ***histidase*** also appear in serum under these conditions.

L22 ANSWER 53 OF 56 CAPLUS COPYRIGHT 2003 ACS

1959:52087 Document No. 53:52087 Original Reference No. 53:9422e-g Tryptophan peroxidase-oxidase, ***histidase***, and transaminase activity in the liver of the developing rat. Auerbach, V. H.; Waisman, Harry A. (Univ. of Wisconsin, Madison). J. Biol. Chem., 234, 304-6 (Unavailable) 1959.

AB cf. ***Cancer*** Research 18, 543(1958). The activities of tyrosine (.alpha.-ketoglutarate), phenylalanine (pyruvate), phenylalanine (.alpha.-ketoglutarate) transaminases, tryptophan peroxidase-oxidase, and ***histidase*** were detd. in the livers of rats of various ages from before birth to about 3 months of age. The 3 transaminase activities appeared at birth. Both phenylalanine and tyrosine transaminases were high at birth but were lower by the 21st day. The tryptophan peroxidase-oxidase system could not be demonstrated in untreated animals before 12 days of age. Injection of tryptophan 5 hrs. before the animals were killed indicated that the animals synthesized small amts. of

tryptophan peroxidase-oxidase during the period when this enzyme was not detected in untreated rats. ***Histidase*** activity was low from 1 to 16 days, but an increase followed which was more rapid in females than in males.

L22 ANSWER 54 OF 56 CAPLUS COPYRIGHT 2003 ACS

1953:19975 Document No. 47:19975 Original Reference No. 47:3460a-c Normal and pathological histidine metabolism in human subjects. Baur, H. (Med. Univ. Klinik, Basel, Switz.). Z. ges. exptl. Med., 119, 143-94 (Unavailable) 1952.

AB The normal imidazole (I) content of the urine of healthy subjects varied between 10 and 80 mg. %, av. 28 mg. %, calcd. as histidine (II). Amts. up to 175, 95, and 75-80 mg. % occurred in cases of liver cirrhosis or dystrophy, virus hepatitis, and advanced exsudative pleuritis, resp. The av. I was 47 and 62 mg. % in 10 ***cancer*** cases and 20 pregnancy cases, resp. Oral intake of more than 250 mg./kg. body wt. l-II increased urinary I. Oral intake of d-II gave an av. recovery in the urine of 76% as I. The ***histidase*** activity in livers without primary parenchymal damage was equiv. to 4-20 ml. 0.02 N NH4OH (cf. Edlbacher, et al., C.A. 37, 401.9); larger values were found in cases of liver damage. Blood I in healthy subjects averaged 4.2 mg. %. After intravenous l- or d-II, blood II decreased rapidly, but with some delay for the d isomer. Slow intravenous infusion of l- or d-II did not affect the plasma histamine level; rapid injection (1 min.) gave a 3-4 fold increase.

L22 ANSWER 55 OF 56 CAPLUS COPYRIGHT 2003 ACS

1939:65561 Document No. 33:65561 Original Reference No. 33:9433b-e Biochemical study on the course of liver ***cancer*** induced by feeding dimethylaminoazobenzene. Masayama, Tatunori; Iki, Hidetane; Yokoyama, Tuneko; Hasimoto, Masaharu Gann, 32, 303-6 (Unavailable) 1938.

AB Changes in chem. substances in the liver of rats were detd. during ingestion of dimethylaminoazobenzene, 1st in the initial stage with little hyperemia, 2nd in the stage of hypertrophy and 3rd in the stage of ***cancer*** production. ***Histidase*** is scarcely present in ***cancer*** tissue. The amt. of arginase is decreased in the ***cancer*** stage. The ascorbic acid content in the initial stage and stage of hypertrophy is increased, but it is decreased in the tumor stage. The glutathione in the liver is increased in the 1st stage. The highest value is found in the tissue next to the cancerous tissue. The tumor tissue has high glutathione content, but its necrotic portion has smaller glutathione content. In the initial stage, the free cholesterol is increased. In the stage of hypertrophy, the ester-cholesterol is increased, and in the tumor stage, the free cholesterol and ester-cholesterol show high values. In the blood plasma, cholesterol increase parallels the increase of cholesterol in the liver. In the stage of ***cancer*** production the increase of free cholesterol is greater than that of ester-cholesterol.

L22 ANSWER 56 OF 56 CAPLUS COPYRIGHT 2003 ACS

1939:1415 Document No. 33:1415 Original Reference No. 33:213f-h Histidine excretion in urine. Tschopp, W.; Tschopp, H. Biochem. Z., 298, 206-26 (Unavailable) 1938.

AB The histidine excretion was detd. in 300 patients. Histidinuria occurs both in males and females in health and in ***disease***, but especially frequently in liver pathology or allergic condition. In pregnancy the histidinuria is quite generally present but cannot be relied on either in diagnosing pregnancy or in excluding it. No relation exists between histidinuria and diet, but in all probability it is connected with the ***histidase*** and histaminase enzyme system. At the present time no definite conclusions would be justified either as to the cause or significance of the urinary histidine. The authors give a very detailed discussion of the method for histidine detn.

=> D L23 6,35 CBIB ABS

L23 ANSWER 6 OF 62 CAPLUS COPYRIGHT 2003 ACS

1995:465731 Document No. 122:205181 Method and apparatus for ***treatment*** of tumors by selective modulation of amino acids in extracorporeal blood. Tepic, Slobodan (AO-Forschungsinstitut, Switz.). PCT Int. Appl. WO 9504560 A1 19950216, 51 pp. DESIGNATED STATES: W: AT,

· AU, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, ES, FI, GB, HU, JP, KP, KR, KZ, LK, LU, LV, MG, MN, MW, NL, NO, NZ, PL, PT, RO, RU, SD, SE, SK, UA, US, UZ, VN; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, DE, DK, ES, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG. (English). CODEN: PIXXD2. APPLICATION: WO 1994-EP2640 19940809. PRIORITY: US 1993-104984 19930810.

AB A method of ***treatment*** of tumors is described which is based on a fundamental dynamic difference between the normal and tumor cells, which underscores the very danger of tumors - their propensity to grow and proliferate under conditions where normal cells would not do so. The preferred mode of ***treatment*** is by extracorporeal blood conditioning, whereby the concn. of one of the set (essential) amino acids is the control parameters. The blood is passed through a filter where the blood cells and the high mol. wt. constituents are sepd. from a plasma fraction contg. low mol. wt. substances, including amino acids. The fraction with low mol. wt. substances is reacted against either absorption or decomp. agents and returned to the blood. The filtration is done to decrease the concn.; increase is controlled by simply injecting the amino acid. A single ***treatment*** session includes at least four phases whereby the concn. is first decreased (collecting all cells in the G0 phase); then increased (pushing the tumor cells over restriction point); then decreased to min. level possible (killing the tumor cells); and finally normalized. Diagrams of the app. are included.

L23 ANSWER 35 OF 62 CAPLUS COPYRIGHT 2003 ACS

1978:577040 Document No. 89:177040 Programming of hepatic ***histidase*** following prenatal administration of diethylstilbestrol. Lamartiniere, C. A.; Lucier, G. W. (Natl. Inst. Environ. Health Sci., Research Triangle Park, NC, USA). Journal of Steroid Biochemistry, 9(7), 595-8 (English) 1978. CODEN: JSTBBK. ISSN: 0022-4731.

AB Oral administration of diethylstilbestrol to pregnant rats at the 15th day of gestation and subsequent measurements of the sex-dependent activities of liver ***histidase*** in these offspring revealed no effect on ***histidase*** activities in immature male and female and adult male offspring. However, ***histidase*** activities of the adult female offspring were decreased and activities approached those of normal adult male. This masculinization of ***histidase*** activity was reversed by exogenously administered 17.beta.-estradiol.

=> S HISTIDINOL

549 HISTIDINOL
1 HISTIDINOLS

L24 549 HISTIDINOL
(HISTIDINOL OR HISTIDINOLS)

=> S L7 AND L24

L25 8 L7 AND L24

=> D 1-8 CBIB ABS

L25 ANSWER 1 OF 8 CAPLUS COPYRIGHT 2003 ACS

2001:781102 Document No. 135:328746 Cloning, overexpression and therapeutic uses of bioactive ***histidine*** ***ammonia*** ***lyase*** from Corynebacteriaceae. Sethuraman, Natarajan; Roberts, Joseph; MacCallister, Thomas (ME Medical Enzymes A.-G., Switz.). PCT Int. Appl. WO 2001079469 A2 20011025, 98 pp. DESIGNATED STATES: W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG, TR. (English). CODEN: PIXXD2. APPLICATION: WO 2001-US12053 20010413. PRIORITY: US 2000-PV197770 20000414.

AB ***Histidine*** ***ammonia*** ***lyase*** isolated from Corynebacteriaceae can decrease serum histidine levels, induce accumulation of urocanic acid, and is not inhibited by L-***histidinol***. A full-length gene and encoded amino acid sequences of ***histidine*** ***ammonia*** ***lyase*** from

Corynebacteriaceae are disclosed. As a result, ***histidine***
ammonia ***lyases*** similar to the one isolated from
Corynebacteriaceae are uniquely suitable for combination therapy with L-
histidinol to treat histidine- and/or histamine-dependent
pathologies, for example, infectious viruses, such as human Respiratory
Syncytial Virus (RSV), Herpes Simplex Virus (HSV), and Human
Immunodeficiency Virus (HIV), as well as cancers.

L25 ANSWER 2 OF 8 CAPLUS COPYRIGHT 2003 ACS

2001:634532 Document No. 136:242628 Nucleotide sequence and predicted
functions of the entire *Sinorhizobium meliloti* pSymA megaplasmid.
Barnett, Melanie J.; Fisher, Robert F.; Jones, Ted; Komp, Caridad; Abola,
A. Pia; Barloy-Hubler, Frederique; Bowser, Leah; Capela, Delphine;
Galibert, Francis; Gouzy, Jerome; Gurjal, Mani; Hong, Andrea; Huizar,
Lucas; Hyman, Richard W.; Kahn, Daniel; Kahn, Michael L.; Kalman, Sue;
Keating, David H.; Palm, Curtis; Peck, Melicent C.; Surzycki, Raymond;
Wells, Derek H.; Yeh, Kuo-Chen; Davis, Ronald W.; Federspiel, Nancy A.;
Long, Sharon R. (Department of Biological Sciences, Stanford University,
Stanford, CA, 94305, USA). Proceedings of the National Academy of
Sciences of the United States of America, 98(17), 9883-9888 (English)
2001. CODEN: PNASA6. ISSN: 0027-8424. Publisher: National Academy of
Sciences.

AB The symbiotic nitrogen-fixing soil bacterium *Sinorhizobium meliloti*
contains three replicons: pSymA, pSymB, and the chromosome. We report
here the complete 1354,226-nt sequence of pSymA. In addn. to a large
fraction of the genes known to be specifically involved in symbiosis,
pSymA contains genes likely to be involved in nitrogen and carbon metab.,
transport, stress, and resistance responses, and other functions that give
S. meliloti an advantage in its specialized niche.

L25 ANSWER 3 OF 8 CAPLUS COPYRIGHT 2003 ACS

2001:634531 Document No. 136:258038 Analysis of the chromosome sequence of
the legume symbiont *Sinorhizobium meliloti* strain 1021. Capela, Delphine;
Barloy-Hubler, Frederique; Gouzy, Jerome; Bothe, Gordana; Ampe, Frederic;
Batut, Jacques; Boistard, Pierre; Becker, Anke; Boutry, Marc; Cadieu,
Edouard; Dreano, Stephane; Gloux, Stephanie; Godrie, Therese; Goffeau,
Andre; Kahn, Daniel; Kiss, Erno; Lelaure, Valerie; Masuy, David; Pohl,
Thomas; Portetelle, Daniel; Puhler, Alfred; Purnelle, Benedicte;
Ramsperger, Ulf; Renard, Clotilde; Thebault, Patricia; Vandenbol,
Micheline; Weidner, Stefan; Galibert, Francis (Laboratoire de Biologie
Moleculaire des Relations Plantes-Microorganismes, Unite Mixte de
Recherche (UMR) 215 Centre National de la Recherche Scientifique (CNRS),
Institut National de la Recherche Agronomique, Chemin, Tolosan, F-31326,
Fr.). Proceedings of the National Academy of Sciences of the United
States of America, 98(17), 9877-9882 (English) 2001. CODEN: PNASA6.
ISSN: 0027-8424. Publisher: National Academy of Sciences.

AB *Sinorhizobium meliloti* is an .alpha.-proteobacterium that forms
agronomically important N₂-fixing root nodules in legumes. We report here
the complete sequence of the largest constituent of its genome, a 62.7%
GC-rich 3654,135-bp circular chromosome. Annotation allowed assignment of
a function to 59% of the 3341 predicted protein-coding ORFs, the rest
exhibiting partial, weak, or no similarity with any known sequence.
Unexpectedly, the level of reiteration within this replicon is low, with
only two genes duplicated with more than 90% nucleotide sequence identity,
transposon elements accounting for 2.2% of the sequence, and a few hundred
short repeated palindromic motifs (RIME1, RIME2, and C) widespread over
the chromosome. Three regions with a significantly lower GC content are
most likely of external origin. Detailed annotation revealed that this
replicon contains all housekeeping genes except two essential genes that
are located on pSymB. Amino acid/peptide transport and degradn. and sugar
metab. appear as two major features of the *S. meliloti* chromosome. The
presence in this replicon of a large no. of nucleotide cyclases with a
peculiar structure, as well as of genes homologous to virulence
determinants of animal and plant pathogens, opens perspectives in the
study of this bacterium both as a free-living soil microorganism and as a
plant symbiont.

L25 ANSWER 4 OF 8 CAPLUS COPYRIGHT 2003 ACS

1993:534183 Document No. 119:134183 Inactivation of ***histidine***
ammonia - ***lyase*** from *Streptomyces griseus* by dicarbonyl
reagents. White, Peter J.; Kendrick, Kathleen E. (Dep. Microbiol., Ohio

State Univ., Columbus, OH, 43210, USA). Biochimica et Biophysica Acta, 1163(3), 273-9 (English) 1993. CODEN: BBACAQ. ISSN: 0006-3002.

AB ***Histidine*** ***ammonia*** - ***lyase*** from *Streptomyces griseus* was inactivated by methylglyoxal and phenylglyoxal, dicarbonyl reagents known to react specifically with arginyl residues in proteins. The inactivation showed pseudo-first-order kinetics and could be prevented by protection with ***histidinol*** phosphate, a competitive inhibitor of ***histidine*** ***ammonia*** - ***lyase***. Anal. of the amino acid compn. of ***histidine*** ***ammonia*** - ***lyase*** after treatment with phenylglyoxal, together with the kinetics of inactivation, suggested that inactivation was a consequence of specific reaction with one or more essential arginyl residues at or near the active site of the enzyme.

L25 ANSWER 5 OF 8 CAPLUS COPYRIGHT 2003 ACS

1993:250244 Document No. 118:250244 ***Histidine*** ***ammonia*** - ***lyase*** from *Streptomyces griseus*. Wu, Pen Chaur; Kroening, Terry A.; White, Peter J.; Kendrick, Kathleen E. (Dep. Microbiol., Ohio State Univ., Columbus, OH, 43210, USA). Gene, 115(1-2), 19-25 (English) 1992. CODEN: GENED6. ISSN: 0378-1119.

AB ***Histidine*** ***ammonia*** - ***lyase*** (***histidase*** ; HutH) has been purified to homogeneity from *S. griseus* and the N-terminal amino acid (aa) sequence used to clone the ***histidase*** -encoding structural gene, hutH. The purified enzyme shows typical satn. kinetics and is inhibited competitively by D-histidine and ***histidinol*** phosphate. High concns. of K.cntdot.cyanide inactivate HutH unless the enzyme is protected by the substrate or ***histidinol*** phosphate. On the basis of the nucleotide sequence, the hutH structural gene would encode a protein of 53 kDa with an N terminus identical to that detd. for the purified enzyme. Immediately upstream from hutH is a region that strongly resembles a class of *Streptomyces* promoters active during vegetative growth; however, there is no obvious ribosome-binding site adjacent to the hutH translation start codon. The deduced aa sequence of an upstream partial open reading frame shows no similarity with other proteins, including HutP of *Bacillus subtilis* and HutU of *Pseudomonas putida*. Promoter-probe anal. indicates that promoter activity maps within the DNA surrounding the hutH start codon. Pairwise comparisons of the primary structures of bacterial and mammalian ***histidases***, together with the unique kinetic properties and gene organization, suggest that streptomycete ***histidase*** may represent a distinct family of ***histidases***.

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1993:186719 Document No. 118:186719 Purification of ***histidase*** from *Streptomyces griseus* and nucleotide sequence of the hutH structural gene. Wu, Pen Chaur; Kroening, Terry A.; White, Peter J.; Kendrick, Kathleen E. (Dep. Microbiol., Ohio State Univ., Columbus, OH, 43210-1292, USA). Journal of Bacteriology, 174(5), 1647-55 (English) 1992. CODEN: JOBAAY. ISSN: 0021-9193.

AB ***Histidine*** ***ammonia*** - ***lyase*** (***histidase***) was purified to homogeneity from vegetative mycelia of *S. griseus*. The enzyme was specific for L-histidine and showed no activity against the substrate analog, D-histidine. ***Histidinol*** phosphate was a potent competitive inhibitor. ***Histidase*** displayed satn. kinetics with no detectable sigmoidal response. Neither thiol reagents nor a variety of divalent cations had any effect on the activity of the purified enzyme. High concns. of potassium cyanide inactivated histdase in the absence of its substrate or ***histidinol*** phosphate, suggesting that, as in other ***histidases***, dehydroalanine plays an important role in catalysis. The N-terminal amino acid sequence of ***histidase*** was used to construct a mixed oligonucleotide probe to identify and clone the ***histidase*** structural gene, hutH, from genomic DNA of the wild-type strain of *S. griseus*. The cloned DNA restored the ability of a ***histidase*** structural gene mutant to grow on L-histidine as the sole nitrogen source. The deduced amino acid sequence of hutH shows significant relatedness with ***histidase*** from bacteria and a mammal as well as phenylalanine ammonia-lyase from plants and fungi.

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1976:401633 Document No. 85:1633 ***Histidine*** ***ammonia*** -

lyase from rat liver. Purification, properties, and inhibition by substrate analogs. Brand, Larry M.; Harper, Alfred E. (Coll. Agric. Life Sci., Univ. Wisconsin, Madison, WI, USA). Biochemistry, 15(9), 1814-21 (English) 1976. CODEN: BICHAW. ISSN: 0006-2960.

AB ***Histidine*** ***ammonia*** - ***lyase*** (I) from rat liver was purified >250-fold to near homogeneity. Electrophoretic detns. indicated a native mol. wt. of .apprx.200,000. The enzyme had a pH optimum of .apprx.8.5. The min. Km for L-histidine was 0.5 mM at pH 9.0. The Km in the physiol. pH range was, however, >2.0 mM. D-.alpha.-hydrazinoimidazolypropionic acid was a potent competitive inhibitor of liver I; the L enantiomer of this compd. was less effective in this regard. The enzyme was also inhibited competitively by L-histidine hydroxamate (Kis = 0.4 mM), and to a lesser extent by L-***histidinol***, D-histidine, and glycine. Failure of a wide variety of other histidine analogues to inhibit the enzyme substantially indicates high specificity of the active site for L-histidine. No alternate substrates were identified for the enzyme. DL-.alpha.-hydrazinophenylpropionic acid, the .alpha.-hydrazino analog of phenylalanine, was a very potent competitive inhibitor of a mechanistically similar L-phenylalanine ammonia-lyase purified from Rhodotorula glutinis. The properties of I from rat liver differed significantly from those of the enzyme from Pseudomonas fluorescens, which has been studied most extensively to date.

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1965:76259 Document No. 62:76259 Original Reference No. 62:13537d-f Bursts of enzyme synthesis in the bacterial duplication cycle. Kuempel, Peter L.; Masters, Millicent; Pardee, Arthur B. (Princeton Univ., Princeton, NJ). Biochem. Biophys. Res. Commun., 18(5-6), 858-67 (English) 1965.

AB cf. CA 60, 13614a. Explorations were made of bursts of enzyme syntheses under normal growth conditions in CS 101-G-1, a guanine auxotroph of Escherichia coli, and in Bacillus subtilis to elucidate why enzyme-formation potential (defined as the max. ability for enzyme synthesis, such as should be obtained by complete derepression), while always present, is expressed only intermittently under normal growth conditions, and how it differs from the autogenous rate of enzyme synthesis (i.e., the amt. of enzyme elaborated/min. in a growing culture). A model was described to explain the results. Potential existed at all times for the synthesis of all enzymes examd. (alk. phosphatase, aspartic transcarbamylase, dihydroorotase, .beta.-galactosidase, ***histidase***, ***histidinol*** dehydrogenase, tryptophanase), changing abruptly at different times for each enzyme. Bursts of autogenous enzyme synthesis were also demonstrated, some enzymes being synthesized continuously, while others were not. Details were given of 1 of several explanations devised for these bursts of autogenous enzyme synthesis by employing a simple model of enzyme repression based on interactions of changing potentials, degrees of repression, and diln. of the system by growth.

=> S L7 AND L8

L26 2 L7 AND L8

=> S L26 NOT (L22 OR L25)

L27 1 L26 NOT (L22 OR L25)

=> D CBIB ABS

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1979:551304 Document No. 91:151304 Biologic and antineoplastic effects of enzyme-mediated in vivo depletion of L-glutamine, L-tryptophan, and L-histidine. Roberts, Joseph; Schmid, Franz A.; Rosenfeld, Henry J. (Sloan-Kettering Inst. Cancer Res., Rye, NY, 10580, USA). Cancer Treatment Reports, 63(6), 1045-54 (English) 1979. CODEN: CTRRDO. ISSN: 0361-5960.

AB Novel enzymes, capable of depleting L-glutamine [56-85-9] plus L-asparagine [70-47-3], L-tryptophan [73-22-3], were purified from soil isolate organisms. L-Glutaminase-L-asparaginase (I) [39335-03-0] from Pseudomonas 7A demonstrated substantial antineoplastic activity against a variety of L-asparaginase-resistant leukemias (L1210, EARAD/1/AR, and C1498), an ascites tumor (Taper liver tumor), and solid tumors (B16 melanoma and Walker 256 carcinosarcoma). I from Pseudomonas 7A was

considerably more potent antitumor agent than I from *Acinetobacter*. Tumors did not develop resistance to I as they do to *Escherichia coli* L-asparaginase (EC-2). Resistance to EC-2 by E6RAD/1 leukemia cells developed in treatment of 2 generations. By contrast, after treatment of 10 generations with I, E6RAD/1 leukemia cells were just as sensitive to both L-glutaminase-L-asparaginase and EC-2 as the parent tumor. Combination therapy with I plus methotrexate [59-05-2] or azaserine [115-02-6] appeared promising. Indolyl-3-alkane .alpha.-hydroxylase [63363-76-8], which attacks the side chain of L-tryptophan, serotonin, and other 3-substituted indole compds., caused marked depletion of L-tryptophan and serotonin [50-67-9] in body fluids and certain tissues. This enzyme exhibited significant antineoplastic activity against a variety of mouse tumors: Meth A sarcoma, Ehrlich carcinoma, and Taper liver tumor. An L- ***histidase*** [***9013-75-6***], which had near-optimal activity in the physiol. pH range and a Km of 1 mM, was isolated from a soil organism belonging to the ***Corynebacteriaceae***. The plasma half-life of this L- ***histidase*** in mice was .apprx.8 h. Treatment of tumor-bearing mice with 500 IU L- ***histidase*** /kg/day maintained plasma L-histidine at unmeasurably low levels (<3 nmol/mL) and resulted in inhibition of total packed cell vol. of the ascitic forms of Ehrlich carcinoma and Meth A sarcoma.